

CLAIMS

We claim:

1. A method for targeting and altering, by homologous recombination, a pre-selected target DNA sequence in a eukaryotic cell to make a targeted sequence modification, said method comprising introducing into at least one eukaryotic cell at least one recombinase and at least two single-stranded targeting polynucleotides which are substantially complementary to each other and each having a homology clamp that substantially corresponds to or is substantially complementary to a preselected target DNA sequence. G
2. A method according to claim 1 further comprising identifying a target cell having a targeted DNA sequence modification at a preselected target DNA sequence.
3. A method according to claim 1, wherein said targeting polynucleotides are coated with said recombinase.
4. A method according to claim 1, wherein said eucaryotic cell is a plant cell.
5. A method according to claim 1, wherein said eucaryotic cell is a mammalian cell.
6. A method according to claim 1, wherein said eucaryotic cell is a zygote.
7. A method according to claim 1, wherein said eucaryotic cell is an embryonic stem cell. B
8. A method according to claim 1, wherein said eucaryotic cell is an avian cell.
9. A method according to Claim 1, wherein said recombinase is a species of prokaryotic recombinase.
10. A method according to Claim 8, wherein said prokaryotic recombinase is a species of prokaryotic recA protein.
11. A method according to Claim 10, wherein said recA protein species is *E. coli* recA.

12. A method according to claim 1, wherein said recombinase is a species of eukaryotic recombinase.
13. A method according to claim 12, wherein said recombinase is a Rad51 recombinase.
- 5 14. A method according to claim 12, wherein said eukaryotic recombinase is a complex of recombinase proteins.
15. A method according to Claim 1, wherein said targeting polynucleotide is conjugated to a cell-uptake component.
- 10 16. A method according to Claim 15, wherein said cell-uptake component is conjugated to said targeting polynucleotide by noncovalent binding.
17. A method according to Claim 15, wherein the cell-uptake component comprises an asialoglycoprotein.
18. A method according to Claim 15, wherein the cell-uptake component comprises a protein-lipid complex.
- 15 19. A method according to Claim 15, wherein said targeting polynucleotide is conjugated to a cell-uptake component and to a recombinase, forming a cell targeting complex.
20. A method according to Claim 1, wherein the targeted sequence modification comprises a deletion of at least one additional nucleotide.
- 20 21. A method according to Claim 1, wherein the targeted sequence modification comprises the addition of at least one additional nucleotide.
22. A method according to claim 20 or 21, wherein said complementary single stranded targeting polynucleotides comprise an internal homology clamp.

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34. A method according to Claim 33, wherein the targeted sequence modification is in a human p53 sequence.
35. A method according to Claim 1, wherein each targeting polynucleotide comprises a homology clamp that is less than 1200 nucleotides long.
- 5 36. A method according to Claim 1, wherein the targeting polynucleotide is less than 1200 nucleotides long.
37. A method according to Claim 1, wherein the targeted sequence modification corrects a gene in a cell.
38. A method according to Claim 1, wherein the targeted sequence modification adds a gene to a cell.
- 10 39. A method according to Claim 1, wherein the targeted sequence modification disrupts a gene in a cell.
40. A method according to Claim 1, wherein the targeted sequence modification modifies a gene in a cell.
- 15 41. A method according to claim 40, wherein the gene is the gal T gene associated with xenoreactivity in humans.
42. A method according to claim 1, wherein at least one of said complementary single stranded nucleic acids further comprise a chemical substituent.
43. A method according to claim 42, wherein said chemical substituent is covalently attached to said nucleic acid.
- 20 44. A composition for producing a targeted modification of an endogenous DNA sequence, comprising two substantially complementary single-stranded targeting polynucleotides and at least one recombinase.
45. A composition according to Claim 44, further comprising a cell-uptake component.

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